IN THE SPECIFICATION

Please amend the specification as follows:

Please replace the paragraph beginning at page 7, line 5, as follows:

Performance of a polymorphous analysis on a target gene ~~LJ~~ after amplifying the target gene ~~gent~~ by a quantitative gene amplification method makes it possible to easily and quickly determine the pre-amplification amount and polymorphous composition of the target gene with good quantitativeness.

Please replace the paragraph beginning at page 22, line 4, as follows:

FIG. 3 illustrates probe designs and target nucleic acid designs for studying effects of the distance (the number of bases) between a fluorescent dye (Texas Red) and a quencher substance (Dabcyl) on the emission of fluorescence from a fluorescence emitting probe making use of interaction between the fluorescent dye and the quencher substance. In the top half of Fig. 3, the sequence (5'→ 3') is that of SEQ ID NO: 109. In the bottom half of Fig. 3, the sequence (5'→ 3') is that of SEQ ID NO: 110;

Please replace the paragraph beginning at page 23, line 1, as follows:

FIG. 5 illustrates probe designs, in each of which bases in a deoxyribooligonucletide chain were modified with both fluorescent dye (Texas Red) and quencher substance (Dabcyl), respectively, and target nucleic acid designs. In the top half of Fig. 5, the sequence (5'→ 3') is that of SEQ ID NO: 109. In the bottom half of Fig. 5, the sequence (5'→ 3') is that of SEQ ID NO: 110;

Please replace the paragraph beginning at page 46, line 8, as follows:

It is also preferred to add a helper probe to a hybridization reaction mixture for raising the efficiency of hybridization of the nucleic acid probe of this invention to the hybridization sequence region. In this case, the oligonucleotide of the helper probe can be in an oiigodeoxyribonucleotide, an oligoribonucleotide or an oligonucleotide subjected to similar chemical modification as described above. Examples of the above-described oligonucleotides can include those having the base sequence of (5')TCCTTTGAGT TCCCGGCCGG A(3') (SEQ ID NO: 52) as the forward type and those having the base sequence of (5')CCCTGGTCGT AAGGGCCATG ATGACTTGAC GT(3') (SEQ ID NO: 53) as the backward type or the reverse type. Preferred examples of the chemically-modified oligonucleotide can include 2-O-alkyloligoribonucleotides, notably 2-O-Me-oligoribonucleotide.

Please replace the paragraph at page 66, lines 4-11, as follows:

In the present invention, the nucleic acid probe is hybridized to the target nucleic acid as described above. The intensity of fluorescence emitted from the fluorescent dye is measured both before and after the hybridization, and a ~~an increase or~~ decrease in fluorescence intensity after the hybridization is then calculated. As the ~~increase or~~ decrease is proportional to the concentration of the target nucleic acid, the concentration of the target nucleic acid can be determined.

Please replace the paragraph beginning at page 93, line 2, as follows:

Currently-available examples of the conventional polymorphous method include SSOP (sequence specific oligonucleotide probe) method, RELP (restriction fragment length polymorphism) method, T-RFLP (terminal restriction fragment length polymorphism) method, SSCP (single strand conformation polymorphism analysis) method, MPH method,

CFLP (cleavage fragment length polymorphism) method, SSP (sequence specific primer) method, PHFA (preferential homoduplex formation assay) method, SBT (sequence base typing) method [PCT Ho, Riyo no Tebiki (PCR Methods, Manual for Their Use), Chugai Medical Publishing Co., Ltd. (1998); Tanpakushitsu, Kakusan, Koso (Proteins, Nucleic Acids, Enzymes), 35(17), KYORITSU SHUPPAN CO., LTD. (1990); Jikken Igaku (Laboratory Medicine), 15(7) (special number), Yodosha (1997)]. T-RELP method or CFLP method can be especially suitably applied, although the methods currently used in polymorphous analyses are all usable in the present invention Features of the polymorphous analysis method will hereinafter be described specifically in order.

Please replace the paragraph beginning at page 104, line 2, as follows:

Assuming that the base sequence of a target nucleic acid was (5')GGGGGGAAAAAAAAA(3') (SEQ ID NO: 1) formed of an oligodeoxy-ribonucleotide, synthesis of a nucleic acid probe according to the present invention was conducted in the following order.

Please replace the paragraph beginning at page 104, line 7, as follows:

As the base sequence of the target nucleic acid was (5')GGGGGGAAAAAAAAA(3') (SEQ ID NO: 1), it was possible to readily design the base sequence of the nucleic acid probe as (5')TTTTTTTTTCCCCCC(3') (SEQ ID NO: 48)formed of an oligodeoxyribonucleotide. The nucleic acid probe according to the present invention was designed further as will be described hereinafter. It was decided to label a fluorescent dye, Texas Red, to a phosphate group on the 5' end and a quencher substance, Dabcyl, to an OH group on the 6-C of a base ring of the 6th thymine from the 5' end (Design of Texas Red-(5')TTTTTT(Dabcyl-)TTTCCCCCC(3')) (SEQ ID NO: 48).

Please replace the paragraph beginning at page 104, line 16, as follows:

Using "5'Amino-Modifier C6 Kit" (trade name, product of Glen Research Corporation, VA, U.S.A.), the phosphate group of thymidylic acid was modified with an amino linker (protecting group: MMT). Using "Amino-Modifier C2dT Kit" (trade name, product of Glen Research Corporation, VA, U.S.A.), the OH group on the 6-C of the base ring of thymidine was modified with an amino linker (protecting group: TFA). Using those modified thymidylic acid and thymidine, an oligonucleotide having the following base sequence was synthesized by a DNA synthesizer ("ABI 394") (trade name, manufactured by PerkinElmer Japan Co., Ltd., Japan) . Specifically, it was a deoxyribooligonucleotide having the base sequence of (5')TTTTTTTTTCCCCCC(3') (SEQ ID NO: 48), the phosphate group on the 5' end was modified with the amino linker (protecting group MMT), and the Oil group on the 6-C of the base ring of the 6th thymine from the 5' end was modified with the amino linker (protecting group: TFA). Incidentally, the synthesis of DNA was conducted by the β-cyanoethylphosphoramidat- e method. After the synthesis, elimination of the protecting groups was conducted with 28% aqueous ammonia at 55°C for 5 hours.

Please replace the paragraph beginning at page 109, line 1, as follows:

An oligonucleotide the base sequence of which was (5')GGGGGGAAAAAAAAA(3') (SEQ ID NO: 1) was synthesized in a similar manner as in the synthesis of the above-described oligonucleotide, and provided as a target nucleic acid to which the present invention is applicable.

Please replace the paragraph beginning at page 117, line 11, as follows:

Preparation of a nucleic acid probe to be hybridized to the nucleic acid base sequence 16S rRNA of *Escherichia coli*, namely, having the base sequence of (3')CCGCTCACGC ATC(5') (SEQ ID NO: 111) was conducted as will be described hereinafter.

Please replace the paragraph beginning at page 117, line 16, as follows:

A deoxynucleotide, which had the base sequence of (3')CCGCTCACGC ATC(5') (SEQ ID NO: 111) and contained $-(CH_2)_7-NH_2$ bonded to the OH group on the carbon atom at the 3' position of deoxyribose at the 3' end of the oligodeoxyribonucleotide, was purchased from Midland Certified Reagent Company, TX, U.S.A. From Molecular Probes, Inc., "FluoReporter Kit F-6082" (trade name) was also purchased, which contained not only "BODIPY FL" propionic acid succinimidyl ester but also a reagent for conjugating the compound to the amine derivative of the oligonucleotide. The kit was caused to act on the above-purchased oligonucleotide, whereby a nucleic acid probe labeled with "BODIPY FL" was synthesized for use in this Example.

Please replace the paragraph beginning at page 120, line 18, as follows:

An oligonucleotide, which was to be hybridized to 23S rRNA of Escherichia coli JM109, had a base sequence of (5')CCCACATCGTTTTGTCTGGG(3') (SEQ ID NO: 4) and contained $-(CH_2)_7-NH_2$ bonded to the OH group on the carbon atom at the 3' position of the 5' end nucleotide of the oligonucleotide, was purchased from Midland Certified Reagent Company, U.S.A. as in Example 8. From Molecular Probes, Inc., "FluoroReporter Kit F-6082" (trade name) was also purchased as in Example 8, which contained not only "BODIPY FL" propionic acid succinimidyl ester but also a reagent for conjugating the compound to the amine derivative of the oligonucleotide. The kit was caused to act on the above-purchased oligonucleotider whereby a nucleic acid probe labeled with "BODIPY FLI" was synthesized.

The synthesized product so obtained was purified as in Example 8, whereby the nucleic acid probe labeled with "BODIPY FL" was obtained with a yield of 25% as calculated relative to 2 mM of the starting oligonucleotide.

Please replace the paragraph beginning at page 123, line 9, as follows:

Name	Target deoxyribooligonucleotide
poly a	5'ATATATATTTTTTTTGTTTTTTTTTTTTTT3' (SEQ ID NO: 5)
poly b	5'ATATATATTTTTTTTTGTTTTTTTTTTTTT3' (SEQ ID NO: 6)
poly c	5'ATATATATTTTTTTTTTGTTTTTTTTTTTT3' (SEQ ID NO: 7)
poly d	5'ATATATATTTTTTTTTTTGTTTTTTTTTTT3' (SEQ ID NO: 8)
poly e	5'ATATATATTTTTTTTTTTTGTTTTTTTTTT3' (SEQ ID NO: 112)
poly f	5'ATATATATTTTTTTTCTTTTTTTTTTTTTT3' (SEQ ID NO: 9)
poly g	5'ATATATATTTTTTTTTCTTTTTTTTTTTTT3' (SEQ ID NO: 10)
poly h	5'ATATATATTTTTTTTTTCTTTTTTTTTTTT3' (SEQ ID NO: 11)
poly i	5'ATATATATTTTTTTTTTTCTTTTTTTTTTT3' (SEQ ID NO: 12)
poly j	5'ATATATATTTTTTTTTTTTCTTTTTTTTTT3' (SEQ ID NO: 13)

Please replace the paragraph beginning at page 124, line 1, as follows:

Name	Invention probe
Probe a	3'TATATATAAAAAAAACAA5'-BODIPY FL/C6 (SEQ ID NO: 14)
Probe b	3'TATATATAAAAAAAAACA5'-BODIPY FL/C6 (SEQ ID NO: 15)
Probe c	3'TATATATAAAAAAAAAAC5'-BODIPY FL/C6 (SEQ ID NO: 16)
Probe d	3'TATATATAAAAAAAAAAA5'-BODIPY FL/C6 (SEQ ID NO: 17)
Probe f	3'TATATATAAAAAAAAGAA5'-BODIPY FL/C6 (SEQ ID NO: 18)
Probe g	3'TATATATAAAAAAAAAGA5'-BODIPY FL/C6 (SEQ ID NO: 19)

Probe h 3'TATATATAAAAAAAAAAG5'-BODIPY FL/C6 (SEQ ID NO: 20)

Please replace the paragraph beginning at page 126, line 11, as follows:

Name	Target deoxyribooligonucleotide
poly k	5'TATATATATATTTTTGGGGG3' (SEQ ID NO: 21)
poly l	5'TATATATATATTTTTTGGGG3' (SEQ ID NO: 22)
poly m	5'TATATATATTTTTTTTTGGG3' (SEQ ID NO: 23)
poly n	5'TATATATATTTTTTTTTTGG3' (SEQ ID NO: 24)
poly o	5'TATATATATTTTTTTTTTTG3' (SEQ ID NO: 25)
poly p	5'TATATATATATTTTTCCCCC3' (SEQ ID NO: 26)
poly q	5'TATATATATATTTTTTCCCC3' (SEQ ID NO: 27)
poly r	5'TATATATATTTTTTTTTCCC3' (SEQ ID NO: 28)
poly s	5'TATATATATTTTTTTTTTCC3' (SEQ ID NO: 29)
poly t	5'TATATATATTTTTTTTTTTC3' (SEQ ID NO: 30)
poly u	5'TATATATATTTTTTTTTTTT3' (SEQ ID NO: 31)

Please replace the paragraph beginning at page 127, line 1, as follows:

Name	Invention probe
probe k	3'ATATATATATAAAAACCCCC5'-BODIPY FL/C6 (SEQ ID NO: 31)
probe l	3'ATATATATATAAAAAACCCC5'-BODIPY FL/C6 (SEQ ID NO: 32)
probe m	3'ATATATATATAAAAAAACCC5'-BODIPY FL/C6 (SEQ ID NO: 33)
probe n	3'ATATATATATAAAAAAAACC5'-BODIPY FL/C6 (SEQ ID NO: 34)
probe o	3'ATATATATATAAAAAAAAAC5'-BODIPY FL/C6 (SEQ ID NO: 35)
probe p	3'ATATATATATAAAAAGGGGG5'-BODIPY FL/C6 (SEQ ID NO: 36)
probe q	3'ATATATATATAAAAAAGGGG5'-BODIPY FL/C6 (SEQ ID NO: 37)

probe r 3'ATATATATATAAAAAAAGGG5'-BODIPY FL/C6 (SEQ ID NO: 38)

probe s 3'ATATATATATAAAAAAAAGG5'-BODIPY FL/C6 (SEQ ID NO: 39)

probe t 3'ATATATATATAAAAAAAAAG5'-BODIPY FL/C6 (SEQ ID NO: 40)

probe u 3'ATATATATATAAAAAAAAAA5'-BODIPY FL/C6 (SEQ ID NO: 41)

Please replace the paragraph beginning at page 129, line 6, as follows:

Name	Target deoxyribooligonucleotide
poly W	5'CCCCCCTTTTTTTTTTT3' (SEQ ID NO: 43)
poly X	5'GGGGGGAAAAAAAAAAAA3' (SEQ ID NO: 44)
poly Y	5'TTTTTTCCCCCCCCCCCC3' (SEQ ID NO: 45)
poly Z	5'AAAAAAGGGGGGGGGGG3' (SEQ ID NO: 46)

Please replace the paragraph beginning at page 129, line 12, as follows:

Name	Invention probe
probe w	BODIPY FL/C6-5'AAAAAAAAAGGGGGG3' (SEQ ID NO: 47)
probe x	BODIPY FL/C6-5'TTTTTTTTTCCCCCC3' (SEQ ID NO: 48)
probe y	BODIPY FL/C6-5'GGGGGGGGGAAAAAA3' (SEQ ID NO: 49)
probe z	BODIPY FL/C6-5'CCCCCCCCCTTTTTT3' (SEQ ID NO: 50)

Please replace the paragraph beginning at page 132, line 9, as follows:

An oligonucleotide was purchased from Midland Certified Reagent Company, U.S.A. as in Example 8. The oligonucleotide had a base sequence of (5')CATCCCCACC TTCCT CCGAG TTGACCCCGG CAGTC(3') (35 base pairs; SEQ ID NO: 51) hybridizable specifically to the 16S rRNA base sequence of KYM-7 strain, said base sequence being equivalent to the base sequence ranging from the 1156th base to the 1190th base of the 16S

rRNA of Escherichia coli JM109, contained deoxyribonucleotides at the 1st to 16th bases and the 25th to 35th bases, respectively, and a methyl-modified ribooligonucleotide at the 17th to 24th bases, said methyl-modified ribooligonucleotide being modified with a methyl group (modified with an ether bond) at the OH group on the carbon atom at the 2' position, and was modified with $-(CH_2)_7-NH_2$ at the OH group of the phosphate group at the 5' end. On the other hand, 2-O-Me-oligonucleotide for use in the 2-O-Me probe (a probe formed of a 2-O-Me-oligonucleotide will be simply called "2-O-Me probe") was obtained from GENSET SA, Paris, France by relying upon their custom DNA synthesis services.

Please replace the paragraph beginning at page 133, line 20, as follows:

Using a DNA synthesizer, an oligoribonucleotide having a base sequence of (5')TCCTTTGAGT TCCCGGCCGG(3') (SEQ ID NO: 52) A was synthesized as in the above to provide it as a forward-type hepter probe. On the other hand, an oligoriboxynucleotide having a base sequence of (5')CCCTGGTCGT AAGGGCCATG ATGACTTGAC GT (3') (SEQ ID NO: 53) was synthesized by using a DNA synthesizer, in a similar manner as described above to provide it as a backward-type, in other words, reverse-type helper probe.

Please replace the paragraph beginning at page 138, line 4, as follows:

9) 35-Base oligoribonucleotide: An oligoribonucleotide having a base sequence of (5')CATCCCCACC TTCCTCCGAG TTGACCCCGG CAGTC(3') (SEQ ID NO: 54).

Please replace the paragraph beginning at page 138, line 7, as follows:

10) 17-Base oligoribonucleotide: An oligoribonucleotide having a base sequence of (5')CCTTCCTCCG AGTTGAC(3') (SEQ ID NO: 55).

Please replace the paragraph beginning at page 141, line 23, as follows:

35-nucleotides-chained oligodeoxyribonucleotide 2-O-Me probe for assaying the rRNA of Cellulomonas sp. KYM-7:

(5')CATCCCCACC TTCCTCCGAG TTGACCCCGG CAGTC(3') (SEQ ID NO: 56)

(the underlined portion is modified with a methyl group)

Please replace the paragraph beginning at page 142, line 2, as follows:

36-nucleotide s-chained oligodeoxyribonucleotide 2-O-Me probe for assaying the rrNA of Agrobacterium sp. KYM-8:

(5') CATCCCCACC TTCCTCTCGG CTTATCACCG GCAGTC (3') (SEQ ID NO: 57)

(the underlined portion is modified with a methyl group)

Please replace the paragraph beginning at page 144, line 11, as follows:

Probe a): 5'C(-BODIPY FL)TTTTTTTTTCCCCCCCCC3' (SEQ ID NO: 58)

Probe b): 5'TTTC(-BODIPY FL)TTTTTTCCCCCCCCC3' (SEQ ID NO: 59)

Target nucleic acid c) for Probe a):

5'GGGGGGGGAAAAAAAAAG3' (SEQ ID NO: 60)

target nucleic acid d) for Probe b):

5'GGGGGGGGAAAAAAGAAA3' (SEQ ID NO: 61)

Please replace the paragraph beginning at page 146, line 16, as follows:

Invention probe: 3'TTTTTTTTGGGGGGGGC5'BODIPY FL/C6 (SEQ ID NO: 62)

Target nucleotide No. 1: 5'AAAAAAAACCCCCCCCA3' (SEQ ID NO: 63)

Target nucleotide No. 2: 5'AAAAAAAACCCCCCCCC3' (SEQ ID NO: 64)

Target nucleotide No. 3: 5'AAAAAAAACCCCCCCCI3' (SEQ ID NO: 65)

(I: hypoxanthine)

Target nucleotide No. 4: 5'AAAAAAAACCCCCCCCG3' (SEQ ID NO: 66)

Please replace the paragraph beginning at page 148, line 5, as follows:

One example of a DNA chip model according to the present invention is illustrated in FIG. 12. Firstly, a modified probe and a surface-treated slide glass were provided. The modified probe had been prepared by introducing an amino group onto the OH group on the carbon atom at the 3' position of ribose at the 3' end of the invention probe, 3'TTTTTTTTGGGGGGGGC5'BODIPY FL/C6 (SEQ ID NO: 62), prepared in Example 21. On the other hand, the surface-treated slide glass had been prepared by treating a slide glass on a surface thereof with a silane coupling agent which contained epoxy groups as reactive groups. A solution with the modified probe contained therein was applied in spots onto the surface-treated slide glass by a DNA chip production apparatus, "GMS" 417 ARRAYER" (manufactured by TAKARA SHUZO CO., LTD., Kyoto, Japan). Asa result, the modified probes were bound at the 3' end onto the surface of the slide glass. The slide glass was then placed for 4 hours or so in a closed vessel to bring the reaction to completion. The slide glass was alternately dipped in 0.2% SDS solution and water, twice in each of the solution and water, for about 1 minute each time. Further, the slide glass was immersed for about 5 minutes in a boron solution, which had been prepared by dissolving $NaBH_4$ (1.0 g) in water (300 mL). Shortly after the slide glass was placed for 2 minutes in water of 95°C., the slide glass was alternately dipped in 0.2% SDS solution and water, twice in each of the solution and water, for about 1 minute each time, so that reagents were washed off. The slide glass was-then dried. As a result, a DNA chip according to the present invention was prepared.

Please replace the paragraph beginning at page 150, line 11, as follows:

An oligodeoxyribonucleotide having the base sequence of (5')AAACGATGTG GGAAGGCCCA GACAGCCAGG ATGTTGGCTT AGAAGCAGCC(3') (SEQ ID NO: 67) was synthesized using a DNA synthesizer "ABI 394" (trade name; manufactured by Perkin-Elmer Inc., MA, U.S.A.), and was provided as a target nucleic acid.

Please replace the paragraph beginning at page 151, line 2, as follows:

1)Probe 100 (100% matched):

(5') CCTTCCCACA TCGTTT (3') (SEQ ID NO: 68),

2) Probe-T (1 base mismatched):

(5') CCTTCCCATA TCGTTT (3') (SEQ ID NO: 69),

3) Probe-A (1 base mismatched):

(5') CCTTCCCAAA TCGTTT (3') (SEQ ID NO: 70),

4) Probe-G (1 base mismtached):

(5') CCTTCCCAGA TCGTTT (3') (SEQ ID NO: 71),

5) Probe-TG (2 bases mismatched):

(5') CCTTCCCTGA TCGTTT (3') (SEQ ID NO: 72), and

6) Probe-TGT (3 bases mismatched):

(5') CCTTCCCTGT TCGTTT (3') (SEQ ID NO: 73).

Please replace the paragraph beginning at page 154, line 16, as follows:

An oligodeoxyribonucleotide having a base sequence of (5')CATCGTTTAC GGCGTGGAC(3') (SEQ ID NO: 74) was synthesized using a DNA synthesizer, "ABI 394" (trade name; manufactured by Perkin-Elmer, Corp.). An oligonucleotide, which had been prepared by treating the phosphate group at the 5' end of the oligodeoxyribonucleotide with

phosphatase to form cytosine and then bonding -$(CH_2)_9$-NH_2, to the OH group on the carbon atom at the 5'-position of the cytosine, was purchased from Midland Certified Reagent Company. From Molecular Probes, Inc., "FluoroReporter Kit F-6082" (trade name) was also purchased, which contained not only "BODIPY EL/C6" propionic acid succinimidyl ester but also a reagent for conjugating the compound to the amine derivative of the oligonucleotide. The kit was caused to act on the above-purchased oligonucleotide, whereby Primer 1 of the present invention labeled with "BODIPY FL/C6" was synthesized.

Please replace the paragraph beginning at page 156, line 5, as follows:

Primer 2 composed of an oligodeoxyribonucleotide, which had a base sequence of (5')CCAGCAGCCG CGGTAATAC(3') (SEQ ID NO: 75), and a fluorescent dye ("BODIPY FL/C6") labeled to the 5' end of the oligodeoxyribonucleotide, was prepared with a yield of 50% in a similar manner as in Example 24.

Please replace the paragraph beginning at page 159, line 24, as follows:

b) Primers:

- Forward primer E8F: (5')AGAGTTTGAT CCTGGCTCAG(3') (SEQ ID NO: 76)

- Reverse primer E1492R: (5')GGTTACCTTG TTACGACTT(3') (SEQ ID NO: 77)

Please replace the paragraph beginning at page 160, line 3, as follows:

c) Probe: BODIPY FL-(5')CGGGCGGTGT GTAC(3') (SEQ ID NO: 78) (with the 3' end phosphorylated)

Please replace the paragraph beginning at page 161, line 24, as follows:

An oligodeoxyribonucleotide having a base sequence of (5') CTGGTCTCCT TAAACCTGTC TTG (3') (SEQ ID NO: 79) was synthesized using a DNA synthesizer, "ABI 394" (trade name; manufactured by Perkin-Elmer, Corp.) An oligonucleotide, which had been prepared by treating the phosphate group at the 5' end of the oligodeoxyribonucleotide with phosphatase to form cytosine and then bonding $-(CH_2)_9-NH_2$, to the OH group on the carbon atom at the 5'-position of the cytosine, was purchased from Midland Certified Reagent Company. From Molecular Probes, Inc., "FluoroReporter Kit F-6082" (trade name) was also purchased, which contained not only "BODIPY FL/C6" propionic acid succinimidyl ester but also a reagent for conjugating the compound to the amine derivative of the oligonucleotide. The kit was caused to act on the above-purchased oligonucleotide, whereby Primer KM38+C of the present invention labeled with "BODIPY FL/C6" was synthesized.

Please replace the paragraph beginning at page 163, line 13, as follows:

An oligodeoxyribonucleotide having a base sequence of (5')GGTTGGCCAA TCTACTCCCA GG(3') (SEQ ID NO: 80) was synthesized in a similar manner as in Example 26.

Please replace the paragraph beginning at page 174, line 17, as follows:

The fluorescence quenching probe Eu47F, which was composed of a deoxyribooligonucleotide having the base sequence of (5')CITAACACATGCAAGTCG(3') (I: inosine) (SEQ ID NO: 81) and labeled on the phosphate group at the 5' end thereof with "BODIPY FL" as will be described below, was synthesized by a DNA synthesizer "ABI 394" (trade name, manufactured by Perkin-Elmer Inc., MA, U.S.A.).

Please replace the paragraph beginning at page 174, line 25, as follows:

A deoxyribooligonucleotide the base sequence of which was (5')TTGTACACACCGCCCGTCA(3') (SEQ ID NO: 82) was synthesized.

Please replace the paragraph beginning at page 187, line 6, as follows:

An artificial co-cultivation system of microorganisms was prepared. Using it as a model system, effectiveness of a quantitative polymorphous analysis method was proven. For the experiment, 10 kinds of microorganisms shown in Table 9 were purchased from DSMZ. The individual strains were separately cultivated using Medium 53. From the cultures, cells were collected, and total DNAs were extracted with a kit reagent "ISOGEN" (trade name, product of NIPPON GENE CO., LTD., Tokyo, Japan) in accordance with its protocol. Using Eu47F (CITAACACATGCAAGTCG, I: inosine) (SEQ ID NO: 81) and Eu1392R (TTGTACACACCGCCCGTCA) (SEQ ID NO: 82) as primers, a PCR reaction was conducted on 16s RNA genes as amplification targets. The thus-amplified products of the 10 kinds of 16S rRNA genes were quantitated by "PicoGreen.sup.RdsDNA Quantitatlon Kit" (trade name, product of Molecular Probes, Inc., OR, U.S.A.), and were then separately diluted with sterilized distilled water to give a concentration of 300,000 copies/mL. The thus-diluted solutions were mixed in equal amounts to provide an artificial co-cultivation system model of microorganisms. This artificial co-cultivation system model of microorganisms contained amplified products of 16S rRNA genes of The 10 microorganisms at concentrations of 30,000 copies/mL, respectively. The total concentration of the amplified products of the 16S rRNA genes was, therefore, 330,000 copies/mL.

Please replace the paragraph beginning at page 188, line 8, as follows:

Using the above-described artificial co-cultivation system of microorganisms (the mixed 16S rRNA gene sample) as a target, quantitative PCR was conducted using

fluorescence emitting primers dually modified with Texas Red and Dabcyl. Employed as common primers were Euq7F-modi (CITAACACATGCAAGTCG, I:inosine) (SEQ ID NO: 81) and Eul392R(TTGTACACACCGCCCGTCA) (SEQ ID NO: 82). Eu47F-modi had similar base sequence as Eu47F, but the 9th T from the 5' end was modified with Texas Red and the 9th T was modified with Dabcyl. The modifications with Texas Red and Dabcyl were conducted in a similar manner as in Example 7. As a quantitative PCR apparatus, "icycler" (trade mark, manufactured by Bio-Rad laboratories, Inc., CA, U.S.A.) was used. The first denature as carried out at 95°C for 60 seconds, and PCR cycles were Conducted under the following conditions: denature: 95°C/60 seconds, annealing: 50°C/60 seconds and extension: 72°C/70 seconds. The PCR reaction was terminated in an exponential growth phase such that the initial composition of the genes would not be altered (no PCR bias would be applied). As the concentrations of the primers, Eu47F and Eu1932R were both set at 0.1 μM, respectively, in terms of final concentration. As a DNA polymerase, "TaKaRa TaqTM" (trade name, product of Takara Shuzo Co., Ltd., Kyoto, Japan) was used at a concentration of 0.5 unit/20 μL. The concentration of Mg ions was set at 2 mM. dNTP was added to give a final concentration of 2.5 mM, respectively. Using "AntiTaq body" (trade name, product of Clontech Laboratories, Inc., CA, U.S.A.), "hot-start" PCR was conducted following the maker's instruction manual. As a standard sample for the preparation of a working line, an amplified product of the 16S rDNA gene of E. coli was used. The preparation of the amplified product of the 16S rDNA gene of E. coli was conducted in a similar manner as the above-described artificial co-cultivation system of microorganisms. Subsequent to the preparation of the working line, quantitation of the artificial co-cultivation system of microorganisms was conducted. The gene concentration of the artificial co-cultivation system of microorganisms was adjusted to give a concentration of 300,000 copies/20 μL in terms of absolute count (20 μL: total amount). Measurement of fluorescence was conducted once after

denature and once after annealing in each cycle. Similarly to the quenching rate of fluorescence (%), the emitting race of fluorescence (%) was determined by correcting the hntensity of fluorescence after annealing (at the time of hybridization) with the intensity of fluorescence after denaturation (at the time of dissociation).

Please replace the paragraph beginning at page 194, line 12, as follows:

After the cenome DNA of Paracoccus denitrificans DSM 413 was extracted by using "DNeasy™ Tissue Kit" (trade name, product of QIAGEN GmbH, Hilden, Germany), the 16S rRNA gene was amplified by conventional PCR while using a Primer set consisting of E10F (AGAGTTTGATCCTGGCTCAG: not modified with any fluorescent dye (SEQ ID NO: 84)) and E140OR(GGTTACCTTGTTACGACTT (SEQ ID NO: 85)). PCR amplification products were quantitated, respectively, by using "Pico Green dsDNA Quantitation Kit" (trade name, product of Molecular Probes, Inc., OR, U.S.A.), and a solution containing the 16S rRNA gene at 6 ng/μL was prepared.

Please replace the paragraph beginning at page 194, line 23, as follows:

The base sequence of the fluorescence emitting probe was 5'CTAATCCTTT-(Texas Red)GGCGAT- (Dabcyl)AAATC3' (SEQ ID NO: 83) in which the 9th T from the 5' end was modified with Texas Red and the 15th from the 5' end was modified with Dabcyl. Modifications were conducted in a similar manner as in Example 7. In addition, the 3' end of the probe was phosphorylated to inhibit any extension from the 3' end. As a forward primer and a reverse primer, those employed in conventional PCR were used (E10F, E1400R) (namely, primers not modified with any fluorescent dye). As a real-time PCR apparatus, "iCycler" (trade mark, manufactured by Bio-Rad Laboratories,, Inc., CA, U.S.A.) was used.

Please replace the paragraph beginning at page 197, line 11, as follows:

As the fluorescence emitting probe, the same fluorescence emitting probe as that employed in Example 39 was used. As the fluorescence quenching probe, that having a similar base sequence as the fluorescence emitting probe and modified at the 5' end thereof with "BODIPY FL" was used {(BODIPY FL)-5'CTAATCCTTTGGCGATAAATC3' (SEQ ID NO: 83)}. The modification was conducted in a similar manner as in Example 8. Employed as targets were a base sequence ((5')GATTTATCGC CAAAGGATTA G(3') (SEQ ID NO: 86)), which was 100% complementary with above-described fluorescence emitting probe and fluorescence quenching probe, and a base sequence ((5')GATTTATCGT CAAAGGATTA G(3') (SEQ ID NO: 87)) complementary with above-described fluorescence emitting probe and fluorescence quenching probe except for the inclusion of single nucleotide polymorphism that the 10^{th} C from the 5' end was replaced by T. The probe was added to a final concentration of 100 nM. A synthesized target DNA was added to a final concentration of 400 nM. The composition of a hybridization solution was similar to that employed in Example 12. As the synthesized target DNA, one of two targets furnished for this Experiment was used. The experiment was conducted by adding the solution, which had been prepared beforehand under the above-described conditions, into a fluorescence measuring tube and heating the solution at 0.1°C/sec from 30°C to 80°C, during which measurement of fluorescence was continuously conducted.

Please replace Table 10 appearing on page 201, as follows:

Probe name	Base sequence (SNPs at the underlined position)	Position modified by Texas Red as counted from the 5' end (5' end base: 0^{th})	Position of Dabcyl as counted from the 5' end
WIAF-10544	5'CGCAGCCGAG CATGGAAGA3' (SEQ ID NO: 88)	6	12

WIAF-13038	5'CGCTGCTGCC CTCCGG3' (SEQ ID NO: 89)	5	11
WIAF-10600	5'AAGGGCACGT GCACATGGC3' (SEQ ID NO: 90)	9	15
WIAF-10579	5'CATCGTGGAG ATGCAGCTGA GG3' (SEQ ID NO: 91)	5	11
WIAF-10578	5'CCTGCAGCAT CATCTGTTAC CTCAC3' (SEQ ID NO: 92)	10	16

Please replace Table 11 appearing on page 202, as follows:

Probe name	Base sequence	Remarks
No. 1 100% match target	5'TCTTCCATGC TCGGCTGCG3' (SEQ ID NO: 93)	Not modified
No.1 1 mismatch target	5'TCTTCCATGG TCGGCTGCG3' (SEQ ID NO: 94)	Not modified; mismatched at the underlined position
No.2 100% match target	5'CCGGAGGGCA GCAGCG3' (SEQ ID NO: 95)	Not modified
No.2 1 mismatch target	5'CCGGAGGACA GCAGCG3' (SEQ ID NO: 96)	Not modified; mismatched at the underlined position
No.3 100% match target	5'GCCATGTGCA CGTGCCCTT3' (SEQ ID NO: 97)	Not modified
No.3 1 mismatch target	5'GCCATGTGCA AGTGCCTT3' (SEQ ID NO: 98)	Not modified; mismatched at the underlined position
No.4 100% mismatch target	5'GCCTGCCACG AGGCTCTCC3' (SEQ ID NO: 99)	Not modified
No.4 1 mismatch target	5'GCCTGCCACC AGGCTCTCC3' (SEQ ID NO: 100)	Not modified; mismatched at the underlined position
No.5 100% match target	5'GTGAGGTAAC AGATGATGCT GCAGG3' (SEQ ID NO: 101)	Not modified
No.5 1 mismatch target	5'GTGAGGTAAC AGTTGATGCT GCAGG3' (SEQ ID NO: 102)	Not modified; mismatched at the underlines position

Please replace the paragraph beginning at page 206, line 10, as follows:

As a forward primer, one having the base sequence of 5' CTTGGGGGGGCATATCTG3' (SEQ ID NO: 103) was used. As a reverse primer, on the other hand, one having the base sequence of 5' ACATCCGGCTTTGACTCTCTCT3' (SEQ ID NO: 104) was employed. This primer set can amplify a section (2509 bp) of the human CYP21 gene. The fluorescence emitting probes and the fluorescence quenching probes have base sequences 100% complementary with their corresponding, SNPs-free amplified products. It was, therefore, expected that the intensities of fluorescence from the fluorescent emitting probes and fluorescence quenching probes shown in Table 12 would increase with the corresponding amplified products.

Please replace Table 12 appearing on page 211, as follows:

Probe name	Probe type	Sequence	Position modified by Texas Red as counted from the 5' end (5' end base: 0^{th})	Position of Dabcyl as counted from the 5' end
WIAF-10600-No. 1	Fluorescence emitting probe	5'AAGGGCACGT GCACATGGC3' (SEQ ID NO: 105)	6	12
WIAF-10578-No. 2	Fluorescence emitting probe	5'CCTGCAGCAT CATCTGTTAC CTCAC3' (SEQ ID NO: 106)	5	11
WIAF-10600-No. 3	Fluorescence emitting probe	5'AAGGGCACGT GCACATGGC3' (SEQ ID NO: 107)	9	15
WIAF-10579-No. 4	Fluorescence emitting probe	5'CCTGCAGCAT CATCTGTTAC CTCAC3' (SEQ ID NO: 108)	5	11

Please delete the substitute Sequence Listing filed on November 19, 2001.

Page 228 (Abstract), after the last line, beginning on a new page, please insert the attached substitute Sequence Listing.